REMARKS

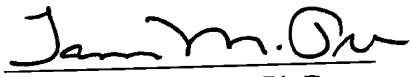
Applicants have amended the specification herein to add sequence identifiers, as suggested by the Examiner in the Notice to Comply with Requirements for Patent Applications Containing Nucleotide Sequences dated August 8, 2003 (copy submitted herewith). No new matter has been added by way of this amendment.

It is noted that the Examiner indicated that a sequence identifier was missing on page 42 of the application. However, Applicants respectfully direct the Examiner's attention to the table on page 42, in which SEQ ID NOS for each sequence are indicated in the first column of the table. Clarification is respectfully requested.

No fees are believed to be due in connection with this Preliminary Amendment. However, please charge any underpayments or credit any overpayments to Deposit Account No. 08-0219.

Respectfully submitted,

HALE AND DORR



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Amendments to the Specification:

Please replace the paragraph spanning page 7, lines 7-8 with the following amended paragraph:

FIG. 1 is a schematic representation of the HCV target mRNA sequence (SEQ ID NO:173) and contiguous oligonucleotides of the invention;

Please replace the paragraph spanning pages 12-13 of the specification with the following amended paragraph:

In another aspect, the present invention provides a synthetic oligonucleotide complementary to at least two non-contiguous regions of an HCV messenger or genomic RNA. Non-contiguous oligonucleotides are targeted to at least two regions of the HCV genomic RNA or mRNA which are not contiguous in a linear sense but, which may be next to each other in three dimensional space due to the secondary structure or conformation of the target molecule (FIGS. 2A and 2B). In preferred embodiments, one or both portions of the non-contiguous oligonucleotide is complementary to the 5' untranslated region. One portion of some non-contiguous oligonucleotides includes the same 12 bases (bases 100-111) designated the "anchor" region. The other portion of such ~~noncontiguous~~ non-contiguous oligonucleotides is variable, containing 6 to 12 bases within, e.g., bases 315-340 of HCV nucleic acid. In one embodiment, one portion which is complementary to the 5' untranslated region comprises the sequence GGGGUCCUGGAG (SEQ ID NO:47), and the other portion is complementary to a 5' region of the RNA encoding the HCV C protein. Other non-contiguous oligonucleotides of the invention may be targeted to other non-contiguous regions of HCV nucleic acid. For example, in another embodiment, the portion which is complementary to the 5' untranslated region and which functions as an anchor comprises the sequence CAACACUACUCG (bases 243-254) (SEQ ID NO:80). In preferred embodiments, the non-contiguous oligonucleotide has about 18 to about 24 nucleotides in length.